

### **Amendments to the Claims:**

The following listing of claims will replace all prior versions of claims in the application:

### **Listing of Claims:**

Claim 1 (currently amended): A self-microemulsifiable base composition, comprising:

a) propofol; and

b) a nonionic surfactant containing polyethylene glycol with the base composition not containing any other nonionic surfactant other than said nonionic surfactant containing polyethylene glycol.

Claim 2 (original): The base composition of claim 1 in which the nonionic surfactant is included in the base composition in a concentration of about eight (8) parts or more of the nonionic surfactant to one (1) part of propofol.

Claim 3 (original): The base composition of claim 1 in which the propofol contains free alpha tocopherol.

Claim 4 (cancelled).

Claim 5 (original): The base composition of claim 1 in which the nonionic surfactant is PEG-660 15 hydroxystearate.

Claim 6 (original): The base composition of claim 1 in which the base composition is anhydrous.

Claim 7 (original): The base composition of claim 1 in which the base composition is homogeneous.

Claim 8 (original): The base composition of claim 1 in which the base composition is optically transparent.

Claim 9 (currently amended): A microemulsion, comprising:

a) the base composition of claim 1, ~~2, 3, 4, 5, 6, 7, or 8~~; and

b) a carrier liquid.

Claim 10 (original): The microemulsion of claim 9 in which the carrier liquid contains water.

Claim 11 (original): The microemulsion of claim 9 in which the carrier liquid is isotonic to blood.

Claim 12 (original): The microemulsion of claim 9 in which the carrier liquid is 0.9% saline in water.

Claim 13 (original): The microemulsion of claim 9 in which the carrier liquid is 5% dextrose in water.

Claim 14 (original): The microemulsion of claim 9 in which the carrier liquid is an isotonic solution containing a crystalloid.

Claim 15 (original): The microemulsion of claim 9 in which the carrier liquid is an isotonic solution containing a colloid.

Claim 16 (original): The microemulsion of claim 9 in which the microemulsion is thermodynamically stable.

Claim 17 (original): The microemulsion of claim 9 in which the microemulsion is optically transparent.

Claim 18 (original): The microemulsion of claim 9 in which the concentration of the propofol is included in the microemulsion in an amount of up to about 1% by weight of the propofol to the volume of the microemulsion.

Claim 19 (original): The microemulsion of claim 9 in which the concentration of the propofol is included in the microemulsion in an amount of up to about 4% by weight of the propofol to the volume of the microemulsion.

Claim 20 (original): The microemulsion of claim 9 which is intravenously injectable into a mammal.

Claim 21 (currently amended): A self-microemulsifiable base composition, comprising:

a) propofol;

b) a nonionic surfactant containing polyethylene glycol with the base composition not containing any other nonionic surfactant other than said nonionic surfactant containing polyethylene glycol;

c) a water-immiscible solvent; and

d) ethanol.

Claim 22 (original): The base composition of claim 21 in which the relative concentration of the nonionic surfactant to propofol included in the base composition is about three (3) to five (5) parts surfactant to about one (1) part propofol, the relative concentration of the water-immiscible solvent to propofol is about three (3) to five (5) parts solvent to about ten (10) parts propofol, and the relative concentration of ethanol to propofol is about five (5) to six (6) parts ethanol to about ten (10) parts propofol.

Claim 23 (original): The base composition of claim 21 in which the relative concentration of the nonionic surfactant to propofol included in the base composition is not less than about three (3) parts surfactant to about one (1) part propofol, the relative concentration of the water-immiscible solvent to propofol is about three (3) to five (5) parts solvent to

about ten (10) parts propofol, and the relative concentration of ethanol to propofol is about five (5) to six (6) parts ethanol to about ten (10) parts propofol.

Claim 24 (original): The base composition of claim 21 in which the propofol contains free alpha tocopherol.

Claim 25 (cancelled).

Claim 26 (original): The base composition of claim 21 in which the nonionic surfactant is PEG-660 15 hydroxystearate.

Claim 27 (original): The base composition of claim 21 in which the water-immiscible solvent is ethyl oleate.

Claim 28 (original): The base composition of claim 21 in which the base composition is anhydrous.

Claim 29 (original): The base composition of claim 21 in which the base composition is homogeneous.

Claim 30 (original): The base composition of claim 21 in which the base composition is optically transparent.

Claim 31 (currently amended): A microemulsion, comprising:

a) the base composition of claim 21, ~~22, 23, 24, 25, 26, 27, 28, 29 or 30;~~

and

b) a carrier liquid.

Claim 32 (original): The microemulsion of claim 31 in which the carrier liquid contains water.

Claim 33 (original): The microemulsion of claim 31 in which the carrier liquid is isotonic to blood.

Claim 34 (original): The microemulsion of claim 31 in which the carrier liquid is 0.9% saline in water.

Claim 35 (original): The microemulsion of claim 31 in which the carrier liquid is 5% dextrose in water.

Claim 36 (original): The microemulsion of claim 31 in which the carrier liquid is an isotonic solution containing a crystalloid.

Claim 37 (original): The microemulsion of claim 31 in which the carrier liquid is an isotonic solution containing a colloid.

Claim 38 (original): The microemulsion of claim 31 in which the microemulsion is thermodynamically stable.

Claim 39 (original): The microemulsion of claim 31 in which the microemulsion is optically transparent.

Claim 40 (original): The microemulsion of claim 31 in which the concentration of the propofol is included in the microemulsion in an amount of up to about 5% by weight of the propofol to the volume of the microemulsion.

Claim 41 (original): The microemulsion of claim 31 in which the concentration of the propofol is included in the microemulsion in an amount of up to about 10% by weight of the propofol to the volume of the microemulsion.

Claim 42 (original): The microemulsion of claim 31 which is intravenously injectable into a mammal.

Claim 43 (previously presented): A method of preparing the ~~microemulsion~~ self-microemulsifiable base composition of claim 9 1 comprising the steps of:

a) heating a predetermined amount of the nonionic surfactant to preparation temperature above its melting point; and

b) combining the nonionic surfactant and a predetermined amount of the propofol, ~~thereby forming the microemulsion.~~

Claim 44 (previously presented): A method of preparing the ~~microemulsion~~ self-microemulsifiable base composition of claim 34 21 comprising the steps of:

a) heating a predetermined amount of the nonionic surfactant to preparation temperature above its melting point; and

b) combining the nonionic surfactant, and predetermined amounts of the water-immiscible solvent, ethanol and propofol, ~~thereby forming the microemulsion.~~

Claim 45 (previously presented): The base composition as in claim 1 in which the non-ionic surfactant has general structure  $[\text{POE}(n)]_{\text{sub}m}\text{-R}'\text{-R}$ ; where POE is a polyoxyethylene moiety (also known as a polyethylene glycol or PEG moiety) of *-mer* number *n*, and having *m* of these POE functional groups attached to R'; where the value of *m* is one to three; where R' is a linking moiety, particularly glyceryl, sorbitan, ester, amino, or ether (oxygen) functions; and where R is a hydrophobic moiety consisting of saturated or unsaturated alkyl or alkylphenyl groups.

Claim 46 (original): The base composition as in claim 45 in which the non-ionic surfactant is selected from the group consisting of polyoxyethylene monoalkyl ethers, polyoxyethylene alkylphenols, polyethylene glycol fatty acid monoesters, polyethylene glycol glycerol fatty acid esters, polyoxyethylene sorbitan fatty acid esters, and polyoxyethylene sterols.

Claim 47 (original): The base composition as in claim 45 in which the structure of the non-ionic surfactant is further defined by a ratio of **A**, the total number of POE *-mer* units in the surfactant (given by the product of *-mer* number **n** and total PEG chain number **m** per molecule); to **B**, the number of carbons in the hydrophobic functional group R, is between about 0.7 and 4, preferably with **A/B** being in the range from about 1 to 2.

Claim 48 (previously presented): The base composition as in claim 47 in which the non-ionic surfactant is selected from the group consisting of **PEG-15** monolaurate, **PEG-20** monolaurate, **PEG-32** monolaurate, **PEG-48** monolaurate, **PEG-13** monooleate, **PEG-15** monooleate, **PEG-20** monooleate, **PEG-32** monooleate, ~~**PEG-15** monolaurate, **PEG-20** monolaurate, **PEG-32** monolaurate, **PEG-48** monolaurate, **PEG-13** monooleate, **PEG-15** monooleate, **PEG-20** monooleate, **PEG-32** monooleate, **PEG-72** monooleate, **PEG-15** monostearate, **PEG-660** 15-hydroxystearate (BASF Corporation's Solutol®), **PEG-23** monostearate, **PEG-40** monostearate, **PEG-72** monostearate, **PEG-20** glyceryl laurate, **PEG-30** glyceryl laurate, **PEG-20** glyceryl stearate, **PEG-20** glyceryl oleate, **PEG-30** glyceryl monooleate, **PEG-30** glyceryl monolaurate, **PEG-40** glyceryl monolaurate, **PEG-20** sorbitan monooleate (polysorbate 80, Tween 80), **PEG-20** sorbitan monolaurate (Tween 20), **PEG-20** sorbitan monopalmitate (Tween 40), and **PEG-20** sorbitan stearate (Tween 60), **PEG-40** sorbitan monooleate, **PEG-80** sorbitan monolaurate, POE-23 lauryl ether, POE-20 oleyl ether, **PEG 30-60** nonyl phenol series (Triton N series), and **PEG 30-55** octyl phenol series (Triton X series, particularly X-305 (POE 30) and X-405 (POE 40).~~

Claim 49 (currently amended): The base composition as in claim ~~1~~ ~~46 or 47~~ in which the non-ionic surfactant has general structure  $[R-(POE)_n]_3$ -glyceride; where POE is a polyoxyethylene moiety (also known as a polyethylene glycol or PEG moiety) of *-mer* number *n*, inserted between fatty acid acyl residues R and a glycerol residue (glyceride), which had, before polyethoxylation, been attached directly to the acyl residues as a common triglyceride.

Claim 50 (original): The base composition as in claim 49 in which the non-ionic surfactant is a polyoxyethylated vegetable oil.

Claim 51 (original): The base composition as in claim 49 in which the structure of the non-ionic surfactant is further defined by a ratio of **A**, the total number of POE *-mer* units in the surfactant (given by the product of *-mer* number *n* and total PEG chain number 3 per molecule); to **B**, the number of carbons in the 3 fatty acid R residues, is between about 0.5 and 3, preferably with **A/B** being in the range from about 0.6 to 1.5.

Claim 52 (original): The base composition as in claim 51 in which the non-ionic surfactant is selected from the group consisting of **PEG-40** palm kernel oil, **PEG-50** hydrogenated castor oil, **PEG-40** castor oil, **PEG-35** castor oil (e.g., Cremaphor®-35), **PEG-60** castor oil, **PEG-40** hydrogenated castor oil, **PEG-60** hydrogenated castor oil, and **PEG-60** corn oil.

Claim 53 (previously presented): The base composition as in claim 21 in which the non-ionic surfactant has general structure  $[POE(n)]_m$ -R'-R; where POE is a polyoxyethylene moiety (also known as a polyethylene glycol or PEG moiety) of *-mer* number *n*, and having *m* of these POE functional groups attached to R'; where the value of *m* is one to three; where R' is a linking moiety, particularly glyceryl, sorbitan,



ester, amino, or ether (oxygen) functions; and where R is a hydrophobic moiety consisting of saturated or unsaturated alkyl or alkylphenyl groups.

Claim 54 (original): The base composition as in claim 53 in which the non-ionic surfactant is selected from the group consisting of polyoxyethylene monoalkyl ethers, polyoxyethylene alkylphenols, polyethylene glycol fatty acid monoesters, polyethylene glycol glycerol fatty acid esters, polyoxyethylene sorbitan fatty acid esters, and polyoxyethylene sterols.

Claim 55 (original): The base composition as in claim 53 in which the structure of the non-ionic surfactant is further defined by a ratio of **A**, the total number of POE *-mer* units in the surfactant (given by the product of *-mer* number **n** and total PEG chain number **m** per molecule); to **B**, the number of carbons in the hydrophobic functional group R, is between about 0.7 and 4, preferably with **A/B** being in the range from about 1 to 2.

Claim 56 (previously presented): The base composition as in claim 55 in which the non-ionic surfactant is selected from the group consisting of **PEG-15 monolaurate**, **PEG-20 monolaurate**, **PEG-32 monolaurate**, **PEG-48 monolaurate**, **PEG-13 monooleate**, **PEG-15 monooleate**, **PEG-20 monooleate**, **PEG-32 monooleate**, ~~**PEG-15 monolaurate**~~, ~~**PEG-20 monolaurate**~~, ~~**PEG-32 monolaurate**~~, ~~**PEG-48 monolaurate**~~, ~~**PEG-13 monooleate**~~, ~~**PEG-15 monooleate**~~, ~~**PEG-20 monooleate**~~, ~~**PEG-32 monooleate**~~, **PEG-72 monooleate**, **PEG-15 monostearate**, **PEG-660 15-hydroxystearate** (BASF Corporation's Solutol®), **PEG-23 monostearate**, **PEG-40 monostearate**, **PEG-72 monostearate**, **PEG-20 glyceryl laurate**, **PEG-30 glyceryl laurate**, **PEG-20 glyceryl stearate**, **PEG-20 glyceryl oleate**, **PEG-30 glyceryl monooleate**, **PEG-30 glyceryl monolaurate**, **PEG-40 glyceryl**

monolaurate, **PEG**-20 sorbitan monooleate (polysorbate 80, Tween 80), PEG-20 sorbitan monolaurate (Tween 20), **PEG**-20 sorbitan monopalmitate (Tween 40), and PEG 20 sorbitan stearate (Tween 60), **PEG**-40 sorbitan monooleate, **PEG**-80 sorbitan monolaurate, POE-23 lauryl ether, POE-20 oleyl ether, **PEG** 30-60 nonyl phenol series (Triton N series), and **PEG** 30-55 octyl phenol series (Triton X series, particularly X-305 (POE 30) and X-405 (POE 40)).

Claim 57 (currently amended): The base composition as in claim 21 ~~54 or 55~~ in which the non-ionic surfactant has general structure  $[R-(POE)_{subn}]_{sub3}$ -glyceride; where POE is a polyoxyethylene moiety (also known as a polyethylene glycol or PEG moiety) of **-mer** number ***n***, inserted between fatty acid acyl residues R and a glycerol residue (glyceride), which had, before polyethoxylation, been attached directly to the acyl residues as a common triglyceride.

Claim 58 (original): The base composition as in claim 57 in which the non-ionic surfactant is a polyoxyethylated vegetable oil.

Claim 59 (original): The base composition as in claim 57 in which the structure of the non-ionic surfactant is further defined by a ratio of **A**, the total number of POE **-mer** units in the surfactant (given by the product of **-mer** number ***n*** and total PEG chain number 3 per molecule); to **B**, the number of carbons in the 3 fatty acid R residues, is between about 0.5 and 3, preferably with **A/B** being in the range from about 0.6 to 1.5.

Claim 60 (original): The base composition as in claim 59 in which the non-ionic surfactant is selected from the group consisting of **PEG**-40 palm kernel oil, **PEG**-50 hydrogenated castor oil, **PEG**-40 castor oil, **PEG**-35 castor oil (e.g., Cremaphor®-35),

**PEG**-60 castor oil, **PEG**-40 hydrogenated castor oil, **PEG**-60 hydrogenated castor oil, and **PEG**-60 corn oil.

Claim 61 (original): The base composition as in claim 21 in which the water-immiscible solvent is a monoester derived from an aliphatic acid and a monoalcohol.

Claim 62 (previously presented): The base composition as in claim 61 in which the monoester is ethyl oleate, ~~propylene glycol dicaprylate~~, isopropyl myristate, ethyl laurate, butyl oleate, oleyl acetate, oleyl propionate, octyl octanoate, octyl decanoate, or oleyl oleate.

Claim 63 (original): The base composition as in claim 21 in which the water-immiscible solvent is a diester derived from a di-alcohol and a mono-acid.

Claim 64 (original): The base composition as in claim 63 in which the diester is propylene glycol dilaurate, propylene glycol dioleate, propylene glycol dicaprylate or 1, 2 butane glycol dioleate.

Claim 65 (original): The base composition as in claim 21 in which the water-immiscible solvent is a diester derived from a di-acid and a mono-alcohol.

Claim 66 (original): The base composition as in claim 65 in which the diester is dioleyl succinate, diethyl fumarate, diethyl malate, or diethyl adipate.

Claim 67 (original): The base composition as in claim 21 in which the water-immiscible solvent is a triester derived from an aliphatic acid and a trialcohol.

Claim 68 (original): The base composition as in claim 67 in which the triester is a triglyceride.

Claim 69 (original): The base composition as in claim 68 in which the triglyceride is glycerol tri-oleate or a medium chain triglyceride oil.

Claim 70 (original): The base composition as in claim 21 in which the water-immiscible solvent is a triester derived from an aliphatic tri-carboxylic acid and a mono-alcohol.

Claim 71 (original): The base composition as in claim 70 in which the triester is a triethyl citrate, tributyl citrate, or triethyl isocitrate.

Claim 72 (original): The base composition as in claim 21 in which the water-immiscible solvent is selected from the group of benzoic acid esters of ethanol, n-propanol, isopropanol, and benzyl alcohol.

Claim 73 (original): The base composition as in claim 21 in which the water-immiscible solvent is oleic acid.

#### **Remarks/Arguments**

Amendments to Claims 1, 9, 21, 31, 43, and 44 are submitted in response to the International Preliminary Report on Patentability, amendments to Claims 45, 48, 49, 53, 56, 57, and 62 are submitted in order to correct certain informalities. Additional amendments to Claims 9 and 31 are submitted in response to the Notification of Insufficient Fees in order to delete the multiple dependent claims and to thereby obviate the need for the payment of additional filing fees.

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